REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. §1.112, are respectfully requested in light of the remarks which follow.

The acknowledgement of the claim for foreign priority and the certified copy is noted, with appreciation. Applicants also appreciate the acknowledgment of the Information Disclosure Statement and return of an initialed copy of applicants' Form PTO-1449.

Claims 1-11, 13, 14, 16, 17, 21, 24, 25, 27-29 and 32-42 are now in this application. Claims 12, 15, 18-20, 22, 23, 26, 30 and 31 have been cancelled by the foregoing amendment, without prejudice or disclaimer, and new Claims 33-42 have been added.

In compliance with the restriction requirement, applicants are no longer pursuing herein composition claims (Group I), claims to a regime or regimen for treating dry skin (Group II), claims to a regime or regimen for treating atopic dermatitis (Group V), or claims to a package (Group IX). Applicants of course reserve the right to file one or more divisional or other continuing applications to pursue the subject matter no longer claimed herein.

Claims 27 and 32 are the only independent claims remaining in the application and are drawn to the elected Group VI invention. All other claims in the application depend, directly or indirectly, from Claim 27 or 32. Claims 1-11, 13, 14, 16, 17 and 21, which were previously composition claims, have been amended so that these claims are now drawn to a regime or regimen; all of these claims depend, directly or indirectly, from independent Claim 27, and therefore now read on the

elected Group VI invention. Claims 24, 25, 28 and 29, which were previously independent regime/regimen claims, have been amended to depend from independent Claim 27. These claims now include all of the limitations of Claim 27, therefore properly fall within the elected Group VI invention. As now worded, they are drawn to the treatment of the indicated conditions only when they are related to a lack of desquamation.

New Claims 33-42 depend, directly or indirectly, from either Claim 27 or Claim 32, thus fall within the elected Group VI invention. Claims 33-34 each specify that the at least one hydrolase polypeptide having amidase activity is at least one compound selected from the group consisting of asparaginase, glutaminase, amidase, urease, aminoacylase, aspartoacylase, ceramidase, peptidyl-glutaminase, formamidase, pentanamidase and aspartylglucosaminidase AGA. These claims are supported by the application as originally filed, in particular by paragraph **[0022]**, which bridges pages 4 and 5 of the specification.

Claims 27 and 32 have been rejected under 35 U.S.C. §112, second paragraph, as indefinite with respect to the phrase "precursor thereof" used with a hydrolase polypeptide. The Examiner considers this unclear. Applicants respectfully disagree. The claims are clear when read in light of the specification by one of ordinary skill of the art. The term "precursor of a peptide" is defined in paragraph **[0024]** of the original specification. In addition, the specification contains information regarding specific embodiments of the precursor; note paragraphs **[0033]**, **[0040]**, and **[0064]** for such particulars. Applicants submit that the use of the expression "precursor thereof" in the claims is thus fully in keeping with the requirements of 35

U.S.C. §112, second paragraph. Withdrawal of the rejection is believed to be in order and is earnestly solicited.

Claims 27 and 32 have been rejected under 35 U.S.C. §102(a) and/or 35 U.S.C. §102(e) as anticipated by Meyers (US2002/0038014 A1) or Rudolph-Owen et al. (WO03/038113 A2). Applicants submit that all of the claims now in the application are free of this rejection.

Meyers teaches two novel asparaginases, 26443 and 46873. While the asparaginases are a family of hydrolases having amidase activity, there are several differences between the cited art and the present invention that should be noted. Meyers suggests the use of asparaginase molecules to deprive malignant cells of the asparagines from extracellular fluid and eventually cause cell death; note **[0053]** of Meyers. This means that the asparaginase is used to inhibit cell proliferation.

Rudolph-Owen et al. designed inhibitors of glycolsylasparaginases (ex.: antisense, antibody), which are known to be sur-expressed in cancers, for inhibiting cellular proliferation and tumoregenesis; see page 2, lines 14-25 of the WO document.

In contrast, applicants claim a method of using a hydrolase polypeptide with amidase activity to promote desquamation of the skin and/or to promote hydration of the skin and/or to promote cell renewal in the skin and/or, in the case of Claim 27 and its dependent claims, for promoting cell proliferation in the skin and/or for promoting cell differentiation in the skin. Indeed, applicants' claims use a hydrolase with amidase activity for promoting desquamation, promoting cell renewal and in the case of Claim 27 and its dependent claims, promoting cell proliferation and/or

promoting cell differentiation in the skin. This is an opposite effect in Claim 27 and 32 from that of the prior art

Furthermore, these prior art documents refer to non-cutaneous cancers such as breast cancer, ovarian cancer, lung cancer and colon cancer (Rudolph-Owens et al.) or carcinoma, sarcoma, metastatic disorders or hematopoietic neoplastic disorders (Meyers). These applications are remote from the treatment of disorders of the skin, particularly skin disorders resulting from a lack of desquamation, which concerns the superficial layer of the skin (stratum corneum). This is the reason that the art does not suggest true topical application but rather systemic drug delivery via parenteral, oral or transdermal administrations.

Moreover, applicants have found surprisingly that aspartylglucosaminidase AGA belonging to the family of hydrolases with amidase activity (EC3.5.1.X) is present in the epidermis in the stratum corneum and has a prodesquamating activity. See, for example, paragraph **[0016]** and Examples 1 and 2 of the instant specification.

Applicants' claims specify applying the hydrolase polypeptide having amidase activity, or precursor thereof, to the skin and promotion of cell renewal or cell proliferation in the skin; moreover, they depend on applicants' discovery of the localization of the enzymes in the skin. One of ordinary skill is not led by the prior art to use of their compounds for treating the skin.

It is also pointed out that applicants' new Clams 33-42 are especially remote from the art, as they specify particular compounds not specifically disclosed by the cited art.

For at least the reasons set forth above, applicants claims cannot possibly be considered to be anticipated by Meyers or Rudolph-Owen et al.

Claim 32 has been rejected under 35 U.S.C. §102(b) as anticipated by the van de Sandt et al. article. Applicants believe that Claim 32 as amended and its dependent claim are free of this rejection.

van de Sandt et al. disclose use of 0.1% sodium dodecyl sulfate (SDS) on human skin to promote cell proliferation. Claim 32 as amended no longer recites promoting cell proliferation and/or cell differentiation in the skin. Thus, Claim 32 as amended and its dependent claim are not anticipated by the van de Sandt et al. article.

For at least the reasons set forth above, it is submitted that the claims are free of all record rejections. Further, favorable action in the form of a Notice of Allowance is believed to be next in order and is earnestly solicited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: October 6, 2005

By: Mary Katherine Baumeister
Mary Katherine Baumeister
Registration No. 26,254

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620